

**Rhône-Poulenc Rorer**

0671 '99 MAR 22 19:02

500 Arcola Road  
PO Box 1200  
Collegeville, PA 19426-0107  
Tel 610-454-8000

March 19, 1999

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
12420 Parklawn Dr.  
Room 1-23  
Rockville, MD 20852

Re: Docket No. 98D-0994  
BACPAC I: Intermediates in Drug Substance Synthesis

Dear Sir:

Reference is made to the draft guidance for industry entitled "BACPAC I: Intermediates in Drug Substance Synthesis" which was published in the Federal Register: November 30, 1998 (Volume 63, Number 229), Docket No. 98D-0994. Rhône-Poulenc Rorer appreciates the opportunity to comment on this draft guidance.

Our comments are as follows:

**General Comment**

- For a site change, the guidance does not differentiate between testing and manufacturing site changes. Rhône-Poulenc Rorer recognizes that the subject of analytical testing laboratories is presented in the guidance document PAC-ATLS: Postapproval Changes - Analytical Testing Laboratory Sites. For purposes of clarity, Rhône-Poulenc Rorer suggests that the BACPAC I document cross-reference the PAC-ATLS document for direction on site changes for analytical testing laboratories.
- In cases where a mechanism for changing suppliers for starting materials is not defined in the NDA, no guidance was found in BACPAC I to indicate how such a change should be reported. Rhône-Poulenc Rorer requests FDA address this issue as part of the finalized guideline.

C 8

98D-0994



### **Stability Testing for New Drug Applications**

- **Lines 123 - 124** state that "The level of impurities should be established by comparing three postmodification batches to the range of historical data from ten premodification commercial batches."

*"Rhône-Poulenc Rorer suggests replacing this line with the following sentence: "The level of impurities should be assessed by comparing three post-modification batches to historical data from a statistically significant number of consecutive pre-modification commercial batches or a combination of consecutive pre-modification batches that includes at least 3 consecutive commercial batches and 3 biobatches, whichever is greater."*

Rhône-Poulenc Rorer makes this suggestion because for some processes of low dose commercially expensive material, the requirement for 10 premodification batches could represent several years of commercial production.

- **Lines 328 - 329** state that "Specification changes for the final intermediate are not included in this guidance." and **Lines 403 - 404** state that "Process changes that result in the formation of a different final intermediate are outside of the scope of this guidance."

Rhône-Poulenc Rorer notes that this different treatment of the final intermediate appears inconsistent with the provision for other changes allowing a sponsor to demonstrate the equivalence on drug substance.

Rhône-Poulenc Rorer hopes that the comments provided will be helpful in finalizing this document. Should you have any questions regarding these comments please feel free to contact me at (610) 454-5498.

Sincerely,

Lelia A. Davenport  
Senior Manager  
Regulatory Affairs - CMC



**FedEx**  
Express  
Shipping  
Label



UBFW 8/97  
PART 151953 Rev. 7/97  
©1994-97 Federal Express Corporation  
Form I.D. No. 0205  
312  
00140/00500 3354882  
Sender's FedEx Account Number 1460-5691-1  
**FedEx**  
FedEx Tracking Number — PULL UP PURPLE TAB  
8019 7908 4076  
8019 7908 4076

☐ For use by PowerShip Customers only

From **Lelia Davenport** Ship Date **3/19/99**

**RHONE-POULENC RORER**  
**500 ARCOLA RD**  
**COLLEGEVILLE PA 19426-0107**

To (If Hold for Pickup, Print FedEx Address Here) (We Cannot Deliver to P.O. Boxes or P.O. Zip Codes.)  
**Dockets Management Branch (HFA-305)**  
**Food and Drug Administration**  
**12420 Parklawn Drive**  
**Room 1-23**  
**Rockville, MD 20852**  
Release No. Phone No. **301-827-1050**

Reference Info	Special Handling	Hold at FedEx Location - Weekday	Hold at FedEx Location - Saturday	Deliver Saturday	Dangerous Goods	Dry Ice
<b>108270</b> FedEx Priority Overnight FedEx Letter <input type="checkbox"/> FedEx Box <input type="checkbox"/> FedEx Pak <input type="checkbox"/> Other Pkg. <input type="checkbox"/>	<b>FedEx Standard Overnight</b> FedEx Letter <input checked="" type="checkbox"/> FedEx Box <input type="checkbox"/> FedEx Pak <input type="checkbox"/> Other Pkg. <input type="checkbox"/>	<b>FedEx 2Day</b> FedEx Letter <input type="checkbox"/> FedEx Pak <input type="checkbox"/> Other Pkg. <input type="checkbox"/>	<b>FedEx First Overnight</b> FedEx Letter <input type="checkbox"/> Other Pkg. <input type="checkbox"/>	<b>FedEx Express Saver</b> FedEx Letter <input type="checkbox"/> FedEx Pak <input type="checkbox"/> Other Pkg. <input type="checkbox"/>	<b>FedEx Overnight Freight</b> Other Pkg. <input type="checkbox"/>	<b>FedEx 2Day Freight</b> Other Pkg. <input type="checkbox"/>

ARVIN DAVIS  
RHONE-POULENC RORER  
500 ARCOLA ROAD  
COLLEGEVILLE PA 19426-0107  
(610)454-3590

SHIP DATE: 19MAR99  
ACC # 146056911  
ACTUAL WGT: 1 LBS MAX-WT

SEE ADDRESS LABEL ON PACKAGE FOR  
THIS SHIPMENT TO MD 20852

8019 7908 4076 **FedEx**

8019 7908 4076

REF: 108270 DAVENPORT

STANDARD OVERNIGHT MON

cad # 0031017 19MAR99

TRK# 8019 7908 4076

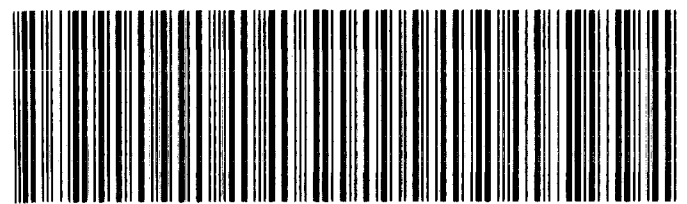
FORM 0201

Deliver by: 22MAR99

IAD AA

20852 -MD-US

**ZMEDGA**



312-1061  
The World On Time®  
3  
m d i c s